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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/769,536	01/30/2004	Zaijie Wang	UIC0002US	8646

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EXAMINER	
KHANNA, HEMANT	
ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 11/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/769,536	WANG, ZAIJIE	
	Examiner	Art Unit	
	Hemant Khanna	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *02/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Examiner acknowledges Applicant's previous cancellation of claims 1-27 in accordance with Examiner's arguments and the addition of new claims 28 and 29, in the reply filed on April 28, 2006. Further, Examiner acknowledges Applicant's election without traverse of claim 28 and cancellation of claim 29 in the reply filed on May 30, 2006.

Applicant's election of species of K93 with traverse in the reply filed on September 05, 2006 is acknowledged. The traversal is on the ground(s) that in an instant application wherein only a generic claim is pending, a restriction between species cannot be required. Further, the Applicant's argue that the species encompassed by the generic claim are related, by virture of being able to inhibit the activity of the calcium calmodulin dependent protein kinase II and is drawing claim to a particular activity which achieves a particular outcome of preventing or reversing the chronic actions of an opium alkaloid.

The restriction between species is maintained. The Applicant's arguments are not found persuasive because while the species are only present in the generic claim, the generic claim 28 recites a genus comprised of a multiplicity of species that an unduly extensive and burdensome search would be necessary to search the entire scope of the claim. See MPEP 803.02. Further, while the Applicant has provided a disclosure of a relationship between species, this is not enough to make them distinct. There exists a patentable difference between the species as claimed. See MPEP

808.01(a). The species of inhibitors of calcium calmodulin dependent kinase II are independent because they are not disclosed as capable of use together. Additionally, the inhibitors are drawn to very different classes of compounds, namely, proteins, small peptides, and synthetic inhibitors, which differ structurally. Further, the synthetic inhibitors can be used in different processes, such as catecholamine biosynthesis, or in the modulation of the production of APP (Amyloid Precursor Protein, USPN 6,043,224). Additionally, the structure searching of the chemical inhibitors and the sequence searches of the protein or small peptide inhibitors do not overlap, and would require a different field of search. Hence, by virtue of the separate classification, non-obvious methods of use, and a divergent field of search, the species of the inhibitors of calcium calmodulin dependent kinase II are distinct.

The requirement is still deemed proper and is therefore made FINAL.

Applicant's elected species is not free of the prior art and the claim 28 that reads on the species stands rejected under 35 USC 102 as set forth below.

Claim 28 is pending.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claim 28 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The specification, while being enabling for methods to modulate the chronic actions of morphine as an opium alkaloid, does not reasonably provide enablement for the prevention or reversal of chronic actions by the administration of calcium calmodulin dependent protein kinase II inhibitors. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or

unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Nature of the invention. The instant invention is to the prevention or reversal of the chronic actions of an opium alkaloid comprising administering to an individual undergoing opium alkaloid therapy an effective amount of a calcium calmodulin dependent protein kinase II inhibitor, namely KN 93.

Breadth of the claims. According to the language of the claims, the use of the inhibitors as claimed would prevent any chronic actions in any animal to any degree.

State and un/predictability of the prior art. The claimed subject matter is lacking in predictability wherein it would at best have invariable results regarding the total prevention or reversal of chronic actions of opium alkaloids at all times. At the time the invention was made, the successful prevention of the chronic actions that resulted from the administration of morphine as an opium alkaloid, was not routinely obtainable by those skilled in the art. It is presumed that the Applicant's intent is to modulate or minimize the tolerance that results from the continued administration of morphine and not prevent the chronic actions of morphine administration. Since the success of the former reads on effectively predicting a condition that will result before the development of tolerance, the prevention is not enabled in view of the contemporary knowledge in the art. This is reflected by the findings in a published manuscript. Gonsalez et al teach that as of 2004, "Pharmacotherapies for heroin addiction may target opiate withdrawal symptoms, facilitate the initiation of abstinence and/or reduce relapse to heroin use either by maintenance on an agonist or antagonist agent. Available agents include

opioid agonists, partial opioid agonists, opioid antagonists, and α-2 agonists for use during managed withdrawal and long-term maintenance" (Abstract, lines 1-5). Further, Gonsalez et al teach that the two major goals of pharmacotherapy are to relieve the severity of opiate withdrawal during managed withdrawal of the opioid, and to prevent relapse to heroin use either after abstinence initiation or after being stabilized on a long-acting opiate agonist, such as methadone" (Abstract, lines 15-19). Since the only relief from opiate withdrawal encompasses initiation of abstinence, or the reduction of relapse to the opioid use, one skilled in the art would conclude that the aspect of preventing the chronic actions of an opioid by the calcium calmodulin dependent protein kinase II cannot be expected in view of the knowledge in the art that suggests that opiate agonists or antagonists as the available options to target the withdrawal symptoms.

Working examples. Although examples are disclosed in the specification that demonstrate reduction in chronic actions of opium alkaloids, no examples indicate the complete reversal of the chronic actions of the opium alkaloid by the administration of KN93 in individuals already tolerant to morphine. Further, no examples are provided that would suggest that the individuals who receive KN93 do not relapse into the chronic actions of the alkaloid therapy.

Guidance in the specification. The specification provides little guidance regarding practice of the claimed methods to extrapolate means of absolute prevention. There is a lack of predictability in the art regarding the prevention of the chronic actions of opium alkaloids. The specification does not explicitly administer other inhibitors belonging to

the same class of compounds as KN93 to yield a preventative endpoint in chronic tolerance to opium alkaloid therapy.

Amount of experimentation necessary. Given the unpredictability of the art in view of prevention of the chronic effects of opium alkaloids by the administration of the calcium calmodulin dependent protein kinase II inhibitors, and the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice the invention commensurate with the scope of the claims. Although the applicants have identified an interesting use of the calcium calmodulin dependent protein kinase II inhibitor namely, KN93 with a role in modulating the chronic effects of opioid therapy, but essentially all of the work required to ultimately develop a prevention method has been left for others.

Relative Skill of those skilled in the art. In view of the discussion of each of the preceding seven factors the level of skill in this art is high and is at least that of a Ph.D. or M.D. with several years of experience in the art. As the cited art would point to, even with a level of skill in the art that is Ph.D. or M.D. predictability of the results is not invariable.

In consideration of each of the factors 1-8, it is apparent that there is undue experimentation because of variability in prediction of outcome that is not addressed by the present application disclosure, examples, teaching and guidance presented. Absent factual data to the contrary, the amount and level of experimentation needed is undue.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claim 28 rejected under 35 U.S.C. 102(b) as being anticipated by Fan G-H et al (Molecular Pharmacology (1999) pages 5639-45).

Instant Claim 28 is drawn to methods of preventing or reversing the chronic actions of an opium alkaloid comprising administering to an individual undergoing opium alkaloid therapy an effective amount of a calcium calmodulin dependent protein kinase II inhibitor, namely KN 93.

Fan G-H et al disclose the administration of KN93 in a saline vehicle by microinjection to rats undergoing morphine therapy (left column, Heading-Materials and Methods, page 40; left column, Heading-Intrahippocampal Administration of KN-93 Attenuated Morphine Tolerance and Dependence). Fan G-H et al further disclose that the animals receiving intrahippocampal injection of KN-93 did so before morphine treatment to inhibit the kinase activity, thus meeting all the limitations of claim 28.

Conclusion

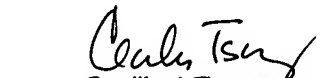
5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Hemant Khanna whose telephone number is (571) 272-9045. The examiner can normally be reached on Monday through Friday, 7:30 am-4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Hemant Khanna
October 24, 2006



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